IN THE CLAIMS: See Listing of Claims attached hereto which will replace all prior versions of claims in the application.

Claims 14 and 19: currently amended.

Claims 17, 18, 20, 23-26: previously presented.

Claim 15: canceled

Claims 27-29: new

The Applicants hereby submit an Information Disclosure Statement, Form PTO-1449, to comply with 37 CFR § 1.98(a)(1). With the instant Office Action, the Office indicates on Form PTO-1449, filed with the Preliminary Amendment of August 22, 2001, that certain references were not considered by the Office. The Applicants hereby submit English language abstracts of International applications and copies of the Chemical Abstracts as required. As will be noted, this Information Disclosure Statement calls a number of references, which might be considered relevant, to the attention of the Office. The fact that these are in fact "prior art" and/or relevant to the prosecution is, however, not admitted. It is understood that, during examination, the Office will make an independent search and will identify any relevant prior art under 37 CFR § 1.104(a).

REMARKS

The Applicants acknowledge the Office Action of July 29, 2004 with appreciation. Claims 14-26 are pending in the application. Of these, Claims 16, 21 and 22 are withdrawn from consideration. The Office has acknowledged election of the invention of Group II, with traverse. Claims 14-15, 17-20 and 23-26 including SEQ ID NO:2 are presently examined.

To begin, the Office rejects Claims 14-15, 17-20 and 23-26 under 35 U.S.C. § 112, first paragraph, for lack of written description. The Office contends that the Applicants have not described a representative number of polynucleotide sequences encoding a TWD protein falling within the scope of the claimed genus of

polynucleotides which are fragments or derivatives of SEQ ID NO:2 or nucleic acids which hybridize to SEQ ID NO:2, and that the Applicants fail to describe structural features common to members of the claimed genus of polynucleotides or the necessary elements essential for the TWD protein. The Office concludes that the Specification fails to provide adequate written description for the broad claim to those fragments, derivatives, or sequences hybridizing with SEQ ID NO:2 which encode a TWD protein.

With the instant Response and Amendment, the Applicants amend Claim 14 to claim an isolated nucleic acid comprising the sequence set forth in SEQ ID NO:2 and non-functional derivatives of SEQ ID NO:2, which fall within the scope of the instant invention. The Office considers the subject matter of SEQ ID NO:2 to be adequately described. With regard to Specificational support for the claim to non-functional derivatives thereof, the Applicants define the term on page 6 of the instant Specification to be a nucleic acid having one or more deletions, substitutions, insertions and/or inversions. The Applicants describe the isolation and sequence analysis of non-functional derivatives. The Applicants submit that any nucleic acid deletion, substitution, inversion, and/or insertion in SEQ ID NO:2 which results in a non-functional nucleic acid, one which does not encode a functional TWD protein, falls within the scope of the claim. The Applicants submit that those skilled in the art are well-versed in manipulating nucleic acid sequences to abolish protein expression from a functional gene, as will be discussed. Additionally, the Specification provides written description and enablement of several non-functional derivatives representative of the genus.

Written description of non-functional derivatives may be found throughout the Specification. The Applicants describe a method for generating non-functional derivatives of SEQ ID NO:2, by introducing a T-DNA insertion. Such methods of generating a mutant nucleic acid by T-DNA insertion are known to those skilled in the art as evidenced by the references cited in the Specification and the Office reference of Babiychuk, et al., (Proc. Natl. Acad. Sci. USA 1997, 94:12722-12727). The Applicants presently reference Hodges, et al., (U.S. Patent 5,527,695) which discloses that the system of T-DNA integration has been extensively described in

the literature and can be modified to introduce foreign genes and other DNA sequences into plant cells (column 3, line 24).

The Applicants also provide description of the isolation and sequence analysis of non-functional derivatives. In Example 4, page 20 of the instant Specification, written description of the structural features of the nucleic acids and functional elements for TWD protein expression are disclosed. The Applicants describe mutations of three non-functional derivatives of SEQ ID NO:2 in detail, disclosing precise genetic alterations and description of those specific regions (e.g., promoter, enhancer, coding regions) of the mutant twisted dwarf nucleic acid sequences which are important for gene expression. Such derivatives are described as having lost promoter, start site, and coding sequence. These non-functional derivatives are disclosed to produce no functional gene product. The Applicants submit that the requirement for written description of representative species encompassed by the scope of the claim has been met, i.e., to SEQ ID NO:2 and non-functional derivatives thereof.

The Office rejects Claims 14-15, 17-20 and 23-24 under 35 U.S.C. § 112, first paragraph, for lack of enablement. The Office opines that the Specification is not enabled for the broad claims to a fragment or derivative of SEQ ID NO:2, or a nucleic acid hybridizing with SEQ ID NO:2, a vector, or method for the production of plants, cells, or seeds comprising said sequence, or methods of homologous recombination. The Office construes that the Specification fails to provide guidance for how to make and/or use the claimed invention and concludes that the Applicant has not reduced the invention to practice.

With the instant amendment, claims are drawn to the isolated nucleic acid of SEQ ID NO:2 and non-functional derivatives thereof. The instant Specification provides an enabling disclosure for the isolation of the nucleic acid of SEQ ID NO:2 in Example 1, page 18, by the method of T-DNA integration and plasmid rescue. The Applicants describe in Example 2, page 18, the use of the nucleic acid set forth by SEQ ID NO:2 to express peptides and generate antibodies to the TWD protein. The Applicants provide detailed protocols for using the claimed nucleic acid sequence for

PCR primer design and PCR amplification of nucleic acid homologues from *Zea mays* and *Lycopersicon esculentum* (Example 5, page 21). Furthermore, in Example 3, page 19 of the instant Specification, the Applicants transform plants with the isolated nucleic acid of SEQ ID NO:2 and demonstrate a phenotypic effect on plant architecture thereby constituting an actual reduction to practice. The Applicants submit that the instant Specification provides an enabling disclosure for the isolation of the nucleic acid sequence set forth in SEQ ID NO:2 and a demonstration of several uses of the nucleic acid to satisfy the enablement requirement.

The Applicants submit that the instant Specification is enabled for the isolation and use of non-functional derivatives. The Specification provides detailed protocols for the generation of derivatives through T-DNA insertion and plasmid rescue. This technique is well-known in the art as evidenced by Hodges, et al. and the cited Babiychuk, et al. The Applicants disclose the isolation and genetic analysis of several derivatives of the *twd* gene, which enabled the isolation of the nucleic acid of SEQ ID NO:2. The Applicants have demonstrated that non-functional derivatives of SEQ ID NO:2, harbored by transgenic plants, exhibit an effect on plant architecture. Thus, the instant Specification discloses multiple examples of how to make and use the isolated nucleic acid of SEQ ID NO:2 and non-functional derivatives thereof and provides a demonstration of reduction to practice. The Applicants submit that compliance with the enablement requirement is met.

The Office opines that the Applicants have not taught how one skilled in the art can use the claimed sequence to generate any of the disclosed phenotypes as listed on page 9, lines 7-20, without undue experimentation.

The Applicants assert that those skilled in the art are familiar with representative techniques used to genetically manipulate plants to exhibit a desired phenotype. This is evidenced by the cited Babiychuk, et al. which disclose insertional mutagenesis by T-DNA vectors. It is discussed in the instant Specification, page 11, line 3, that the instant nucleic acids may be changed to generate inactive derivatives, for example by T-DNA insertion, or through deletion or insertion of DNA

to generate the disclosed phenotypic changes. Additionally, those skilled in the art are well-versed in genetic manipulation of nucleic acid sequences to inactivate gene expression. Written description of the *twd* genomic sequence is found in Figure 1, wherein the nucleic acids of SEQ ID NO:2 which encode the amino acids comprising the TWD protein are identified. Based upon this disclosure, one skilled in the art would be apprised of nucleic acids to contemplate mutations in the coding sequence which would give rise to a non-functional derivative and to formulate DNA constructs for homologous recombination for the creation of transgenic plants mutant for TWD protein expression to give rise to the desired phenotype.

Examples of non-functional derivatives of SEQ ID NO:2 which were isolated from the transgenic plants and analyzed genetically are set forth in Example 4, page 20. The Applicants describe those specific structures of the nucleic acid sequences which are genetically altered to give rise to the twisted dwarf phenotype. Such derivatives are disclosed to have lost promoter, start site, and/or coding sequence. Therefore, those skilled in the art may rely on the Specificational disclosure for guidance as to the manipulation of the instant nucleic acid sequences to generate a non-functional nucleic acid for introduction into plants for the disclosed phenotype. The Specification and references cited therein provide detailed protocols for the generation of mutant plants using T-DNA inactivation. The Applicants discuss the isolation of nucleic acid derivatives and provide genetic analysis and disclosure of the genetic alterations which give rise to non-functional derivatives. The Applicants have demonstrated that transgenic plants harboring non-functional derivatives of SEQ ID NO:2 exhibit the phenotypes described on page 9 of the instant Specification.

Further, the Office concludes that the Specification does not teach how one skilled in the art would use a plant transformed with any of the claimed sequences.

The amended claims are drawn to an isolated nucleic acid of SEQ ID NO:2 and non-functional derivatives thereof. The Applicants have demonstrated an alteration in the wild type plant morphology when transgenic plants harbor non-functional derivatives of SEQ ID NO:2. The Applicants discuss the attributes of plants

transformed with inactive derivatives extensively in the instant Specification, starting on page 4. On page 11 of the instant Specification, it is discussed that transgenic plants with disoriented growth are desired for wood with changed rigidity for desired processing or physical characteristics, and further that transgenic plants may present reduced seed loss during harvesting of siliques. The Applicants have demonstrated that non-functional derivatives of the sequence set forth in SEQ ID NO:2 give rise to plants with the desired phenotype of disoriented growth. The Applicants have demonstrated that this phenotype may then be reversed by expression of the nucleic acid of SEQ ID NO:2. The Applicants submit that the Specification enables the use of plants transformed with the instant nucleic acid or a non-functional derivative thereof.

Those skilled in the art genetically alter plants through introduction of nucleic acid sequences, including homologous recombination. The Applicants, herewith, provide a reference to Hodges, et al., (U.S. Patent 5,527,695) which substantiates this understanding and which rebuts the Office conclusion that homologous recombination in plants is impractical and provides evidence that those skilled in the art are well-versed in making transgenic plants via homologous recombination.

Homologous recombination in plants is the subject matter of the Hodges, et al. disclosure. The reference discloses methods contemplated by those skilled in the art for genetic manipulation of nucleic acid sequences for targeted integration into the host genome via homologous recombination (Column 4, line 1). Those skilled in the art are familiar with the requirements for gene expression and are well-versed in manipulation of nucleic acids to express or repress the activity of a gene. Therefore, the Specificational teaching and the teaching of those skilled in the art provide a written description and enablement for the use of the instant nucleic acids to generate plants, through homologous recombination or T-DNA insertion, exhibiting the phenotypes disclosed on page 9 of the instant Specification.

The Applicants submit that the Specificational teaching to isolate and use nucleic acids which confer the desired growth characteristics, as well as the experimental/procedural teaching of Babiychuk, et al. and Hodges, et al., provide

one skilled in the art with an enabling disclosure. Consequently, the Specification is enabled for SEQ ID NO:2 and non-functional derivatives thereof. Reconsideration and withdrawal of the rejection is respectfully solicited.

Moving on, the Office rejects Claims 14 and 15 under 35 U.S.C. §101 as being directed to non-statutory subject matter. The Applicants amend Claim 14 to add clarifying language which refers to an "isolated" nucleic acid, as kindly suggested by the Office.

The Office rejects Claims 14-15 and 17-18 under 35 U.S.C. 102(b) as being anticipated by Peattie, et al., (U.S. Patent No. 5,763,590). Peattie, et al. disclose a nucleic acid sequence that encodes an FK506 binding protein which exhibits sequence similarity to the instant nucleic acid of SEQ ID NO:2 and which the Office concludes would hybridize under low stringent conditions.

The Applicants submit that the instant amendment, defining the claim scope to the sequence set forth in SEQ ID NO:2 and non-functional derivatives thereof distinguishes over the cited prior art. This subject matter is not anticipated by Peattie, et al. Reconsideration and withdrawal of the prior art rejection is respectfully requested.

The Office rejects Claims 14-15 and 17-18 under 35 U.S.C. 102(b) as being anticipated by Holt, KA., (U.S. Patent No. 5,886,791). Holt discloses a non-analogous protein. The Office finds Holt to teach expression of cDNA in plants. The Applicants submit that the instant amendment, defining the claim scope to SEQ ID NO:2 and non-functional derivatives thereof, is not anticipated by the reference disclosure. Reconsideration and withdrawal of the prior art rejection is respectfully solicited.

The Applicants add new Claim 27 drawn to the isolated nucleic acid of SEQ ID NO:2 which encodes a polypeptide of the sequence set forth in SEQ ID NO:3.
Also, new Claims 28 and 29 are added to include clarifying language as to the orientation of the claimed nucleic acid sequences relative to the transcriptional

regulatory elements. Specificational support for the amendment is found on page 10, line 12 where it is disclosed that the claimed nucleic acids may be integrated and expressed in an antisense orientation. Consequently, this language may not be considered to be new matter.

* * * * *

The Office raises objections to the Specification and Drawings for several clerical or translational errors. With the instant Response and Amendment, the Applicants provide the necessary corrections in the enclosed replacement paragraphs provided in the Amendments to the Specification pages. Annotated Marked-up Drawings and corresponding Replacement Sheets of the Drawing Figures are also enclosed. The Replacement Sheets include a correction of the figure labels for Figures 1-3.

* * * * *

Accordingly, reconsideration of all grounds of objection and rejection, withdrawal thereof, and passage of this application to issue are all hereby respectfully solicited.

It should be apparent that the undersigned attorney has made an earnest effort to place this application into condition for immediate allowance. If he can be of assistance to the Examiner in the elimination of any possibly-outstanding insignificant impediment to an immediate allowance, the Examiner is respectfully invited to call him at his below-listed number for such purpose.

Allowance is solicited.

Respectfully submitted,

THE FIRM OF HUESCHEN AND SAGE

By: 

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Enclosure: Listing of Claims; Amendments to the Specification; Annotated Marked-up Drawings; Replacement Sheets; Information Disclosure Statement, Form PTO-1449; Accompanying References; Extension fee, three months; Check in the amount of $1020.00 and Postal Card Receipt.

* * * * *

THE COMMISSIONER IS HEREBY AUTHORIZED TO CHARGE ANY FURTHER OR ADDITIONAL FEES WHICH MAY BE REQUIRED (DUE TO OMISSION, DEFICIENCY, OR OTHERWISE), OR TO CREDIT ANY OVERPAYMENT, TO DEPOSIT ACCOUNT NO. 08,3220.

Annotated Marked-up Drawings. ~~4/4~~

~~Figur 1A~~

Figure 1.

```
1     GTCTAAGAACCTTAAGGAGAAAGAGATTAAGAGGCAGACATTGCTTGAGCTTGTTGATTA
61    TGTTGCATCAGTTGGTTTTAAGTTTAACGATGTTTCGATGCAAGAGTTAACGAAGATGGT
121   AGCGGTTAATCTGTTTAGAACTTTTCCTTCTGCGAATCACGAGAGTAAAATTCTTGAAAT
181   ACATGATATGGATGATGAAGAACCTTCTTTGGAGCCAGCTTGGCCTCATGTTCAAGTTGT
241   GTATGAGATTCTTCTCAGATTCGTGGCTTCTCCCATGACTGATGCAAAGCTTGCCAAGAG
301   ATATATTGACCATTCTTTTGTCTTGAAGCTCTTAGACTTGTTTGATTCTGAAGATCAAAG
361   AGAGAGGGAATATCTAAAAACTATTCTGCATCGGGTGTACGGGAAGTTCATGGTGCATCG
421   ACCTTACATCAGAAAGGCGATAAACAATATCTTCTACAGATTCATATCCGAGACTGAAAA
481   GCATAATGGCATTGCGGAGTTGCTAGAGATTCTTGGAAGTATAATTAATGGTTTTGCTTT
541   GCCTTTAAAAGAAGAGCACAAGCTCTTCCTTTTGCGAGCCTTGATTCCTCTCCACAAGCC
601   TAAATGTTCATCAGTCTATCACCAACAGCTTTCGTATTGCATTGTTCAGTTTGTAGAAAA
661   GGACTTCAAGCTCGCTGATACCGTTATTAGAGGTCTTTTAAAATATTGGCCTGTGACTAA
721   CAGCTCAAAGGAAGTTATGTTTCTTGGAGAGTTAGAAGAAGTCTTGGAAGCAACTCAAGC
781   CGCTGAGTTTCAACGTTGTATGGTTCCATTATCCCGACAAATTGCTCGATGCCTCAACAG
841   TTCACATTTCCAGGTTCGAGTCTTTGACTATCATCACAACTTCATATCTATCTCTCTTGA
901   TAAAGTCTTGTACCTATATATGAAGTTGTACTTTTTGTTTGTCAGGTTGCTGAAAGAGCA
961   TTGTTTCTATGGAACAACGATCACATAAGAAACCTGATCACTCAGAACCATAAAGTGATA
1021  ATGCCTATAGTCTTCCCAGCTCTTGAGAGAAACACGCGTGGACATTGGAACCAAGCAGTT
1081  CAAAGTCTGACTATAAACGTGAGGAAAGTATTATGCGAGATTGACCAAGTTCTTTTCGAC
1141  GAGTGTTTAGCCAAATTCCAAGTAGAAGAAGTGAATAAAACAGAGGTTAAAGCGAAACGG
1201  GAAAGGACATGGCAACGGTTAGAAGATTTAGCTACTTCAAAGACCGTTGTAACCAACGAG
1261  GCAGTACTGGTTCCAAGATTTGTGTCCTCAGTCAATCTTACTACAAGCAGCTCTGAGTCC
1321  ACAGGGTCGTAGTAGGCTCTCGTAGGTTACTATGTACTTGTAACAAATATTTGTGGTCAC
1381  TATAGAAATGGTTCTTGAGAGACGACTGTATAATTATTTTTTTAAATTATAATCTTTTGG
1441  GTCAAATTGAGAATATTTGATATTATTTTACTGAATTATAATAAACGCCGTTAAAACTCT
1501  CGTTAGTTAACGGCTGACTCTGAAGTGAAAACTGAAAAGTCGAAGGGTCTCTTTATATTT
1561  TCAGAATCAAAATCTGAAATTTATCTCTCGGTCGATCCAGTCTTCGTGAGTGACTTCGAC
1621  GACGACGACGAGTCACACTACTCTTGAGCTTCTCATACTTCGTAAGTTCACTCTCCTCTT
1681  CTCTAAATTGACAAACTTTTTCTTCGTTTTCTGCTATTATTGACGACGAGACTTGATTTT
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Annotated Marked-up Drawings.

~~2/4~~

~~Figur 1B~~

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1741 GTTTTGAAATGAAATGGTTCAAGTAGCTGACTTCGACTATGTTCTTTTGGGTTTTTGTCA

1801 TTGAATCTTACTTGTCTGATTTGGTCGATGTTTAATCAATTCAACACTTAAAGATTCAAT

1861 TTTTGGATTGACACTTGCACATTTTTATTCAGACCCAGGTTGATTTGGGAAATAATGGAT
                                                          M  D   2

1921 GAATCTCTGGAGCATCAAACTCAAACACATGGTAAGTAAATTTTCATAGATTTAATCTCT
     E  S  L  E  H  Q  T  Q  T  H  D                          13

1981 CTGAATACATATATATGACTTCAATATGTTTGATTGGAGTTTTTTTGTTGTCCCATATTC

2041 AATTGGATGCTTTGTTAAAGGATAAATGTCTATCAAATTATGTTGACTGCGTTATTCTTT

2101 CTAAATCATATTGTGAATCTTGGAACAAAGCATGTATACAACAAATTTGTTAGACTTAAT

2161 AACTCCTTTTCTGTTTGTTAAGAATTGAGAATGACTATTGGGGTTGACTAATGCATCTTT

2221 TGTGGCTCCAGACCAAGAGAGCGAAATAGTTACTGAAGGAAGTGCCGTTGTGCATAGTGA
                    Q  E  S  E  I  V  T  E  G  S  A  V  V  H  S  E  29

2281 GCCATCTCAAGAGGGTAATGTTCCTCCTAAAGTTGATAGTGAAGCTGAGGTCTTGGATGA
     P  S  Q  E  G  N  V  P  P  K  V  D  S  E  A  E  V  L  D  E  49

2341 GAAAGTCAGTAAGCAGATTATAAAGGAAGGTCACGGTTCCAAACCATCCAAGTACTCTAC
     K  V  S  K  Q  I  I  K  E  G  H  G  S  K  P  S  K  Y  S  T  69

2401 ATGCTTTTGTAAGTACCCTTTAGCTTTCTGTTGATTGGATGTTGATTTTTCGATTGCACT
     C  F  L                                                     72

2461 TGTTGGCCTATTGCTACTGTTTATTTGAATCTTTCTATCTGACCAATTTCATATTGGCCA

2521 TAGTGCACTACAGGGCATGGACCAAAAACTCGCAGCACAAATTTGAGGATACATGGCATG
          H  Y  R  A  W  T  K  N  S  Q  H  K  F  E  D  T  W  H  E  91

2581 AGCAGCAACCTATTGAATTGGTTCTTGGAAAAGGTATGTGGCTGTCGAATATGTACTCTA
     Q  Q  P  I  E  L  V  L  G  K  E                            102

2641 CACCTCCATTTCGTTAGATGAATCGTCATTGGTAAATTTGATGAGTTAGCTTGTGTATTA

2701 TATGAACCCAATGAGATGGATATTTGGGAGGAAAAAAGATTGAGTTTTGTATTTTTTTTG

2761 CTTCAATGCTGATTAGCCCATTTTAACGTCACTATACAATTTTTTTTATAAAAAAGATTG

2821 TGCACTAAGAGTGAAATGTTGTCTGTGAGACAGAGAAAAAAGAACTAGCCGGTTTAGCCA
                                        K  K  E  L  A  G  L  A  I  111

2881 TCGGTGTTGCTAGCATGAAGTCTGGTGAACGTGCGCTTGTGCATGTTGGCTGGGAATTAG
     G  V  A  S  M  K  S  G  E  R  A  L  V  H  V  G  W  E  L  A  131

2941 CTTATGGGAAAGAAGGAAACTTTTCTTTTCCCAATGTTCCACCTATGGCAGACTTGTTAT
     Y  G  K  E  G  N  F  S  F  P  N  V  P  P  M  A  D  L  L  Y  151

3001 ATGAGGTGGAAGTTATTGGGTTTGATGAAACAAAGGAGGTAAGTTATTTCCTATACCATC
     E  V  E  V  I  G  F  D  E  T  K  E                         163
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~~Figur 1C~~

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3061 ATCTTGTTTCCTTACCAAGACGACTCCACATCCAAGCTTTATCCCAACCTCCTTGCTTAC

3121 CTCTCTGACTTAGATGATGTATTGAACAGGGAAAAGCTCGCAGTGATATGACTGTAGAGG
                                    G  K  A  R  S  D  M  T  V  E  E 174

3181 AAAGGATTGGTGCAGCAGACAGAAGAAAAATGGATGGGAATTCTCTTTTTAAGGAGGAGA
       R  I  G  A  A  D  R  R  K  M  D  G  N  S  L  F  K  E  E  K 194

3241 AACTGGAGGAAGCCATGCAACAGTATGAAATGGTTATGCATCTCTCTCTATCTCTATCTC
       L  E  E  A  M  Q  Q  Y  E  M                                204

3301 TCTTTCCAACAATTACGGTCAAAGTTTAGGTTTTCAGGCATACTTAGTGAGTCTGCTCGA

3361 GGCTCTTGTGTCTTCTTTCGGCTTTTGATTAGTCATGGTTTTGCTGTTTCAGGCCATAGC
                                                        A  I  Y  207

3421 ATACATGGGGGACGATTTTATGTTTCAGCTGTATGGGAAGTACCAGGATATGGCTTTAGC
       Y  M  G  D  D  F  M  F  Q  L  Y  G  K  Y  Q  D  M  A  L  A 227

3481 AGTTAAAAACCCATGCCATCTTAACATAGCAGCTTGCCTCATCAAACTAAAACGATACGA
       V  K  N  P  C  H  L  N  I  A  A  C  L  I  K  L  K  R  Y  D 247

3541 TGAAGCAATTGGTCACTGCAACATTGTAAGACTCATCAAACCATTCATTTGAAGAAAATC
       E  A  I  G  H  C  N  I                                      255

3601 ATTAAAGTTCATACTCGGTTTCTCGAAATCTAATCAAACTCAAAACCTTATCAGGTGTTG
                                                        V  L  257

3661 ACAGAAGAAGAGAAAAACCCAAAAGCACTGTTCAGAAGAGGGAAAGCAAAGGCAGAGCTA
       T  E  E  E  K  N  P  K  A  L  F  R  R  G  K  A  K  A  E  L  277

3721 GGACAGATGGACTCAGCACGTGATGATTTCCGAAAGGCACAAAAGTATGCTCCTGACGAC
       G  Q  M  D  S  A  R  D  D  F  R  K  A  Q  K  Y  A  P  D  D  297

3781 AAGGCGATTAGAAGAGAGCTACGAGCACTTGCAGAGCAAGAGAAAGCCTTGTACCAAAAG
       K  A  I  R  R  E  L  R  A  L  A  E  Q  E  K  A  L  Y  Q  K  317

3841 CAGAAAGAAATGTACAAAGGAATATTCAAAGGGAAAGATGAAGGTGGTGCTAAGTCAAAG
       Q  K  E  M  Y  K  G  I  F  K  G  K  D  E  G  G  A  K  S  K  337

3901 AGCCTTTTTTGGTTGATAGTGTTATGGCAATGGTTTGTTTCCCTTTTCTCCCGTATCTTT
       S  L  F  W  L  I  V  L  W  Q  W  F  V  S  L  F  S  R  I  F  357

3961 CGACGCCACAGAGTTAAAGCAGATTAATGTATGAAGAAGGGTTACAATTA
       R  R  H  R  V  K  A  D  *                                   365
351    SLFSRIFRRH RVKAD
```
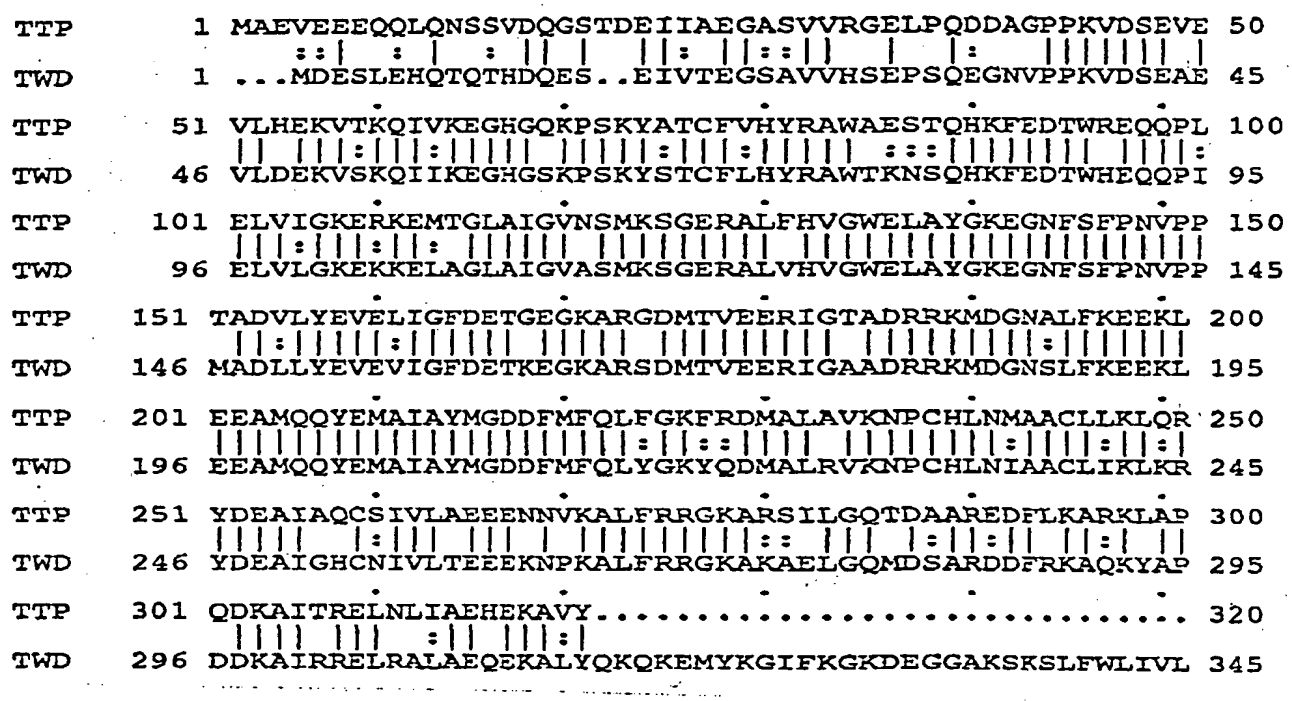

Annotated Marked-up Drawings.

~~FIGURE 2~~

Figure 2.



~~FIGURE 3~~

Figure 3.